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## Letter to the Editor

**Comparison of hospital treatment strategy or of treatment actually received in COVID-19?**

**Commenting on: Lammers AJJ, Brohet RM, Theunissen REP, Koster C, Rood R, Verhagen DWM, et al. Early hydroxychloroquine but not chloroquine use reduces ICU admission in COVID-19 patients. *Int J Infect Dis.* 2020 September**

To the editor,

We read with great interest the publication by Lammers et al., in which they report on the effects of hydroxychloroquine (HCQ) and chloroquine (CQ) on on-ward mortality and ICU admission in hospitalised COVID-19 patients (Lammers et al., 2020). We commend the authors for their valuable addition to the existing literature on this much discussed subject. It is a thoroughly analysed retrospective cohort study with great attention for detail. The authors chose a setup to minimise bias by indication. However, the study's methodology, as described in the article, triggers a question with implications for its interpretation.

At several points in the article the authors give the impression that their study design entailed comparing hospital treatment strategies for COVID-19 (i.e., comparing hospitals routinely treating their patients with chloroquine, with hospitals routinely treating with hydroxychloroquine, with hospitals using neither drug as treatment) as opposed to the more commonly used approach of comparing groups of patients receiving these actual treatments. This method approaches the intention-to-treat strategy used in randomised-controlled trials (Brookhart et al., 2006; Greenland, 2000). The following sentences in the abstract seem to suggest that the authors compare hospital strategies: "Hospitals were given the opportunity to decide independently on the use of three different COVID-19 treatment strategies: HCQ or CQ, or no treatment. We compared the outcome among these groups".

However, the study results also suggest that the authors might have compared groups stratified by treatment actually received. For instance, the reported numbers of included patients per group (HCQ, CQ and controls) reported in the abstract and results sections correspond to the numbers in the groups marked as treated in the case of active treatments of HCQ and CQ, and to the aggregate of the untreated patients from all three strategies in the case of the controls. This would indicate that untreated patients in centres routinely using HCQ or CQ were analysed as untreated controls, instead of including them in the HCQ/CQ treatment strategy. The uncertainty in the applied method creates some difficulty to compare outcomes with other similar studies such as our recently published study in a similar setting, where we used a hospital

treatment strategy analysis (Peters et al., 2020). Could the authors please elucidate if they compared hospital strategies or treatment actually received?

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None.

**Conflict of interest**

No conflict of interest to declare.

**Ethical approval**

Approval was not required.

**References**

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